Attorney's Docket No.: 17170-004001 (25835-4003)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Gerardo M. Castillo et al.

Art Unit : 1615

Serial No.: 10/684,178

Examiner: Unknown

Filed

October 10, 2003

Title

: ISOLATION, PURIFICATION, AND SYNTHESIS OF PROCYANIDIN B2 AND

**USES THEREOF** 

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

## TRANSMITTAL LETTER

Transmitted herewith are an Information Disclosure Statement (2 pages); Form PTO-1449 (11 pages); Cited References (1 box containing 4 Volumes); and a return postcard for filing in connection with the above-captioned application

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The Commissioner is hereby authorized to charge any additional fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 06-1050. A duplicate of this

sheet is enclosed.

Respectfully submitted,

Mhungralkar

Megha Bhumralkar Reg. No. 44,536

Date: April 29, 2004

Attorney Docket No. 17170-004001(25835-4003)

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Attorney's Docket No.: 17170-004001 (25835-4003)



Applicant: Gerardo M. Castillo et al.

Art Unit: 1615

Serial No.: 10/684,178

Examiner: Unassigned

Filed

: October 10, 2003

Title

ISOLATION, PURIFICATION, AND SYNTHESIS OF PROCYANIDIN B2 AND

**USES THEREOF** 

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

## INFORMATION DISCLOSURE STATEMENT IN ACCORDANCE WITH 37 C.F.R. 1.97-1.98

Dear Sir:

Because this Information Disclosure Statement is filed before the receipt of a First Office Action on the Merits for the above-captioned application a fee is not required. If no proper payment is enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 06-1050.

In accordance with the duty of disclosure imposed by 37 C.F.R. §1.56 to inform the Patent Office of all references known by Applicant or Applicant's representative that may be material to the examination of the subject application, Applicant's representative hereby provides this Information Disclosure Statement that is prepared in accordance with 37 C.F.R. §§1.97-1.98. Form PTO-1449 (11 pages) and hard copies of the Foreign Patent Documents and Other Art Documents are provided herewith in connection with the above-captioned application.

The documents cited on the Forms PTO-1449 are in the English language with the exception of Item BB. Item BB (Japanese Patent JP 1-151514) is in the Japanese language and is supplied with an English language Derwent Abstract (item CK). Hence, in accordance with the requirements of 37 C.F.R. 1.98, as amended effective March 16, 1992, no further explanation of the listed items is necessary.

Applicant also makes known to the Examiner the following pending U.S applications that have one or more common inventors and/or are commonly owned:

Applicant: Gerardo M. Castillo et al. Attorney's Docket No.: 17170-004001(25835-4003)

Serial No.: 10/684,178 Filed: October 10, 2003

Page : 2 of 2

U.S.S.N.(App.No.)	Filing Date	Publication No.	Pub. Date	Docket No.
09/748,748	12/26/00	2001/0047032	11/29/01	17170-002001 (HEWM; 25835-4001)
10/762,444	01/21/04			17170-002002 (HEWM; 25835-4001B)
10/452,851	05/30/03			17170-003001 (HEWM; 25835-4002)
10/077,596	02/15/02	2003/0017998	01/23/03	17170-006001 (HEWM; 25835-4005)
10/384,172	03/05/03	2003/0233669	12/18/03	
09/036,492	03/06/98			
09/079,829	03/15/98			
09/497,628	02/03/00			
09/296,481	10/02/98			
09/525,787	03/15/00			

Although these documents are made known to the Patent and Trademark Office in compliance with Applicant's duty of disclosure, such disclosure is not to be construed as an admission by Applicant or Applicant's representative that any of the references, singly or in any combination thereof, is effective as prior art against the subject application. In accordance with 37 C.F.R. 1.97(h), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 C.F.R 1.56(b) exists.

Applicant respectfully requests that the Examiner review the foregoing references and they be made of record in the file history of the above-captioned application.

Respectfully submitted,

Bhungalbar

Megha Bhumralkar Reg. No. 44,536

**Dated: April 29, 2004** 

Docket No: 17170-004001 (25835-4003)

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Substitute Form PTO-144 (Modified)

U.S. epartment of Commerce Patent and Trademark Office

Atorney Docket No. 17170-004001(25835-4003) Application No. 10/684,178

List of Patents and Publications for Applicant's Information Disclosure Statement

Applicant

Gerardo M. Castillo et al.

Filing Date

October 10, 2003

Group Art Unit 1615

(37 CFR §1.98	3(b))			15	- · · ·		
ina	Dania	Desument		nt Documents			Filing Data
Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	A	3,536,809	10/27/1970	Applezweig	424	28	2/17/1969
	В	3,598,123	8/10/1971	Zaffaroni	128	268	4/1/1969
	С	3,845,770	11/5/1974	Theeuwes et al.	128	260	6/5/1972
	D	3,916,899	11/4/1975	Theeuwes et al.	128	260	2/7/1974
	Е	4,008,719	2/22/1977	Theeuwes et al.	128	260	2/2/1976
	F	4,710,384	12/1/1987	Rotman	424	465	7/28/1986
	G	5,059,595	10/22/1991	Le Grazie	424	468	3/20/1990
	Н	5,061,629	10/29/1991	Coffen et al.	435	280	10/29/1990
	I	5,073,543	12/17/1991	Marshall et al.	514	21	7/21/1988
	J	5,120,548	6/9/1992	McClelland et al.	424	473	11/7/1989
	K	5,354,556	10/11/1994	Sparks et al.	424	9	7/9/199
	L	5,478,579	12/26/1995	Sawruk	424	535	7/21/199
	M	5,591,767	6/7/1997	Mohr et al.	514	413	6/6/199
	N	5,639,476	6/17/1997	Oshlack et al.	424	468	6/2/199
	O	5,643,562	7/1/1997	Kisilevsky et al.	424	78.31	3/15/199
	P	5,674,533	10/7/1997	Santus et al.	424	493	5/26/199
	Q	5,703,129	12/30/1997	Felsenstein et al.	514	613	9/30/199
	R	5,728,375	3/17/1998	Kilsilevsky et al.	424	78.31	6/6/199
· · · · · · · · · · · · · · · · · · ·	S	5,733,566	3/31/1998	Lewis	424	426	10/30/199
	T	5,767,126	6/16/1998	Marchbanks	514	297	10/18/199
,	U	5,958,883	9/28/1999	Snow	514	- 16	6/5/199
	V	6,037,327	3/14/2000	Castillo et al.	514	23	8/28/199
	W	6,264,994	7/24/2001	Castillo et al.	424	725	12/8/199
- 100 %	x `	6,297,281	10/2/2001	de Lassauniere et al.	514	589	3/2/199
	Y	6,340,783	1/22/2002	Snow	800	12	10/3/199
	Z	6,346,280	2/12/2002	Castillo et al	424	725	11/24/199
	AA	6,432,636	8/13/2002	Maresh et al.	435	6	8/26/199

Examiner Signature

Date Considered

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Form PTO-1449 (Modified)

U.S. Department of Commerce Patent and Trademark Office

Atorney Docket No. 17170-004001(25835-4003) Application No. 10/684,178

List of Patents and Publications for Applicant's **Information Disclosure Statement** 

Applicant Gerardo M. Castillo et al.

Filing Date

October 10, 2003

Group Art Unit 1615

(37 CFR §1.98	3(b))					_	
			U.S. Pater	nt Documents			
Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	AB	6,563,016	5/13/2003	Snow et al.	800	12	3/27/2000
	AC	6,607,758	8/19/2003	Castillo et al.	424	769	8/24/2001
	AD	2001/0047032	11/29/01	Castillo et al.	514	453	12/26/00
	AE	2002/0086067	7/4/2002	Choi et al.	424	729	12/29/2000
·	AF	2002/0111309	8/15/2002	Castillo et al.	514	12	8/22/2001
	AG	2002/0119934	8/29/2002	Castillo et al.	514	23	4/29/2002
	AH	2002/0150637	10/17/2002	Castillo et al.	424	730	3/26/2002
	AI	2002/0150948	10/17/2002	Castillo et al.	435	7.1	11/2/2001
	AJ	2002/0151506	10/17/2002	Castillo et al.	514	27	3/15/2002
	AK	2002/0168753	11/14/2002	Castillo et al.	435	226	11/30/2001
	AL	2002/0197692	12/26/2002	Castillo et al.	435	184	11/2/2001
	AM	2003/0013648	1/16/2003	Castillo et al.	514	12	9/24/2001
	AN	2003/0017998	1/23/2003	Snow et al.	514	27	2/15/2002
	AO	2003/0153734	8/14/2003	Castillo et al.	530	370	12/18/2002
	AP	2003/0233669	12/18/03	Snow et al.	800	18	03/05/03

	Foreig	n Patent Doc	uments or Pu	blished Foreign P	atent A	Application	าร	
Examiner	Desig.	Document	Publication	Country or			1	slation
Initial	ID	Number	Date	Patent Office	Class	Subclass	Yes	No
	AQ	00/12102	3/9/2000	PCT				
	AR	00/30666	6/2/2000	PCT				
	AS	00/33659	6/15/2000	PCT				<u> </u>
	AT	00/55187	9/21/2000	PCT				
	AU	00/57707	10/5/2000	PCT				
	AV	01/49307	7/12/2001	PCT				
	AW	01/56567	8/9/2001	PCT				
	AX	02/062422	8/15/2002	PCT				
	AY	02/076381	10/3/2002	PCT				

**Examiner Signature** 

Date Considered

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Application No. Substitute Form PTO-1449 U.S. Department of Commerce Atorney Docket No. (Modified) Patent and Trademark Office 17170-004001(25835-4003) 10/684,178 Gerardo M. Castillo et al. List of Patents and Publications for Applicant's **Information Disclosure Statement** Filing Date **Group Art Unit** October 10, 2003 1615 (37 CER 81 98(b))

(37 CFR §1.98								
	Foreig	n Patent Doc	uments or Pu	ıblished Foreign P	atent A	Application	าร	
Examiner	Desig.	Document	Publication	Country or			Trans	slation
Initial	ID	Number	Date	Patent Office	Class	Subclass	Yes	No
	AZ	02/41842	5/30/2002	PCT				
	BA	02/42329	5/30/2002	PCT				
	BB	1-151514	6/14/1989	JP				Abstract
	BC	96/28187	9/19/1996	PCT				
	BD	97/46664	12/11/1997	PCT				
	BE	98/09653	3/12/1998	PCT				
	BF	98/15178	4/16/1998	PCT				
	BG	98/34646	8/13/1998	PCT				
	ВН	98/39653	9/11/1998	PCT				
	BI	98/51302	11/19/1998	PCT				
	BJ	99/09999	3/4/1999	PCT				
	BK	99/45947	9/16/1999	PCT				

	Other Documents (include Author, Title, Date, and Place of Publication)				
Examiner	Desig.				
Initial	ID	Document			
	BL	Acheson et al. "The synthesis of some acylglycines and related oxazolones," J. Am. Chem. Soc. Abstracts., pp.3457-61 (1960)			
	ВМ	Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, 4th ed. (Jerry March Ed.) New York: John Wiley & Sons (1992), Chapter 4, pp.94-164			
	BN	Altmann et al., "Effects of the 1,2-Dimenthylhydrazine on the Number of Epithelial Cells Present in the Villi, Crypts, and Mitotic Pool along the Rat Small Intestine," Cancer Research 44:5522-5531 (1984)			
	во	Arai et al, "Argyrophilic glial inclusions in the midbrain of patients with Parkinson's disease and diffuse Lewy body disease are immunopositive for NACP/α-synuclein," Neurosc. Lett. 259:83-86 (1999)			
	BP	Arnaudinaud et al., "Total synthesis of isotopically labelled flavonoids. Part 5: Gram scale production of 13C-labelled (-)-procyanidin B3," Tetrahedron Letters 42:5669-5671 (2001)			
	BQ	Askanas et al., "β-Amyloid Precursor Epitopes in Muscle Fibers of Inclusion Body Myositis," Ann. Neurol. 34: 551-560 (1993)			
	BR	Barner et al. "Donepezil Use in Alzheimer Disease," The Annals of Pharmacotherupy, 32:70-77, (1998)			
	BS	Bell, E.T., "Hyalinization of the islets of langerhans in nondiabetic individuals," Am. J. Pathol. 35:801-805 (1959)			
	вт	Benson et al. "Serum Amyloid a Protein in Amyloidosis, Rheumatic, and Neoplastic Diseases," Arthritis and Rheumatism, 22(1): 36-42, (1979)			
Examiner Sign	nature	Date Considered			

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Atomey Docket No. 17170-004001(25835-4003)	Application No. 10/684,178	
List of Patents and Pub	lications for Applicant's	Applicant Gerardo M. Castillo et al.		
	losure Statement	Filing Date October 10, 2003	Group Art Unit 1615	

(37 CFR §1.98						
		ocuments (include Author, Title, Date, and Place of Publication)				
Examiner Initial	Desig. ID	Document				
	BU	astillo et al. "Sulfate content and specific glycosaminoglycan backbone of perlecan are critical of erlecan't enhancement of islet amyloid polypeptide (Amylin) Fibril formation."Diabetes, 47: 612-20, (1998).				
	BV	Castillo et al., "Laminin inhibition of beta-amyloid protein (A beta) fibrillogenesis and identification of an A beta binding site localized to the globular domain repeat on the laminin a chain", J. Neurosci. Res., 62(3):451-462 (2000)				
	BW	Castillo et al., "The sulfate moieties of glycosaminoglycans are critical for the enhancement beta- amyloid protein fibril formation", J. Neurochem., 72(4):1681-1687 (1999)				
	BX	Castillo. "Novel Purification and detailed characterization of perlecan isolated from the engelbreth-holm-swarm tumor for use in an animal model of fibrillar AB amyloid persistence in brain." J. Biochem. 120(2):433-444, (1996).				
	BY	Castillo. "Perlecan Binds to the β-amyloid proteins (Aβ) of alzheimer's desiase, Accelerates Aβ fibril formation, and Maintains Aβ fibril Stability." Journal of Neuochemistry, 69(6): 2452-2465, (1997).				
	BZ	Cerri et al., "New Quinovic Acid Glycosides from Uncaria Tomentosa," Journal of Natural Products 51(2):257-261 (1988)				
	CA	Chemical abstracts, vol. 50(g), 10 May 1956, column: 6402 by Tamura, Saburo et al. "VI. Syntheses of some w, w'-bis(3,4-dihydroxyphenyl)alkanes .I "Journal of the Agricultural Chemical Society of Japan (Nippon Nogei Kagakukaishi), 27: 491-498 (1953)				
	СВ	Chemical abstracts, vol. 50(g), 10 May 1956, column: 6402 by Tamura, Saburo et al. "VI. Syntheses of some w, w'-bis(3,4-dihydroxyphenyl)alkanes .2"Journal of the Agricultural Chemical Society of Japan (Nippon Nogei Kagakukaishi), 27: 877-881 (1953)				
	CC	Clark et al, "Islet Amyloid, Increased A-Cells, Reduced B-Cells and Exocrine Fibrosis: Quantitative Changes in The Pancreas in Type 2 Diabetes," Diabetes Res. 9:151-159, (1988)				
	CD	Clark et al., "Localisation of islet and amyloid peptide in lipofuscin bodies and secretory granules of human B-cells and in islets of type-2 diabetic subjects," Cell Tissue Res. 257:179-185 (1989)				
	CE	Conway et al., "Accelerated in vitro fibril formation by a mutant α-synuclein linked to early-onset Parkinson disease," Nature Med. 4:1318-1320, (1998)				
	CF	Cooper et al. "Purification and characterization of a peptide from amyloid-rich pancreases of type 2 diabetic patients." Proc. Natl. Acad. Sci. USA, 84:8629-8632, (1987)				
	CG	Crutcher et al., "Cellular and molecular pathology in Alzheimer's disease", Hippocampus, 3:271-287 (1993)				
	СН	Cutler et al. "Correspondence: Tacrine in Alzheimers Disease," The New England Journal of Medicine, pp. 808-810, (Mar. 18, 1993.)				
	CI	Czochanska et al, "Direct Proof of a Homogeneous Polyflavan-3-ol Structure for Polymeric Proanthocyanidins," J.C. S. Chem. Comm. pp. 375-377, (1979)				
	Cì	Davidson et al., "The Effect of Aging on Carbohydrate Metabolism: A Review of the English Literature and a Practical Approach to the Diagnosis Mellitus in the Elderly," Metabolism 28(6):688-705 (1979)				
	CK	Derwent Abstract for Japanese Patent Application, JP 1151514, published 06/14/89, "Compsn. for treating and preventing nervous diseases -contains carboxylic acid, prf. gallic or pyrogallol-4-carboxylic acid, esp. useful for alzheimers disease -contains carb oxylic acis, pref. gallic or pyrogallol-4-carboxylic acid, esp. useful for alzheimers disease ".				

Examiner Signature	Date Considered			
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conformance and not considered. Include copy of this form with next co	mmunication to applicant			

Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Atorney Docket No. 17170-004001(25835-4003)	Application No. 10/684,178	
List of Patents and Publi	ications for Applicant's	Applicant Gerardo M. Castillo et al.		
Information Disclosure Statement		Filing Date October 10, 2003	Group Art Unit 1615	

(37 CFR §1.98	B(b))					
	Other D	ocuments (include Author, Title, Date, and Place of Publication)				
Examiner	Desig.					
Initial	ID	Document  Flotobor et al. "Plant Progentha eveniding Part 3. Conformational and Conformational Studies of				
	CL	Tetcher et al, "Plant Proanthocyanidins. Part 3. Conformational and Configurational Studies of Natural Procyanidins," JCS Perkin 1:1628-1637, (1977)				
		Flood et al. "Amnestic effects in mice of four synthetic peptides homologous to amyloid B protein				
	CM	from patients wit alzheimer disease." Proc. Natl. Acad. Sci. USA, 88:3363-3366 (1991)				
		Flood et al. "An amyloid β-protein fragment, Aβ[12-18], equipotently impairs post-training memory				
	CN	processing when injected into different limbic system structures." Brain Research 663:271-27				
		(1994).				
	СО	Fraser et al., "Conformation and fibrillogenesis of Alzheimer A beta peptides with selected				
		substitution of charged residues", J. Mol. Biol., 244(1):64-73 (1994)				
	CD	Fukuchi et al., "Increased expression of beta-amyloid protein precursor and microtubule-associated				
	СР	protein tau during the differentiation of murine embryonal carcinoma cells", J. Neurochem.,				
		58(5):1863-1873 (1992) Games et al. "Alzheimer-type neuopathology in transgenic mice overexpressing V717F B-amyloid				
	CQ	precursor protein." Nature, 373: 523-527 (1995)				
		Gejyo et al. "A New Form of Protein Associated with Chronic Hemodialysis was Identified as B2				
	CR	Metroglobulin," Biochemical and Biophysical Research Communications, 129(3): 701-706, (1985)				
	CS	Gejyo et al. "β2-Metroglobulin: A New Form of Protein Associated with Chronic Hemodialysis,"				
	CS	Kidney International, 30:385-590 (1986).				
		Glenner et al. "Alzheimer's Disease: Initial Report of the Purification and Characterization of a				
	CT					
		120(3): 885-890 (1984) Grundke-Iqbal et al. "Abnormal Phosphorylation of the Microtubule-Associated Protein Tau				
	CU	Alzheimer Cytoskeletal Pathology," Proc. Natl. Acad. Sci. USA, 83:4913-4917 (1986)				
	GI.	Gujer et al, "Glucosylated Flavonoids and Other Phenolic Compounds From Sorghum,"				
	CV	Phytochemistry 25:1431-1436 (1986)				
	CW	Haass et al. "The swedish mutation causes early-onset alzheimer's disease by β-secretase cleavage				
	CW	with in the secretory pathway." Nature Medicine 1(12):1291-1296 (1995).				
	CX ·	Harada et al. "Human Amyloid Protein: Chemical Variability and Homogeneity," Journal of				
		Histochemistry and Cytochemistry, 19(1): 1-15 (1970)				
	CY	Hardy et al., "Framing β-amyloid", Nature Genet., 1:233-234 (1992)				
	CZ	Harrigan et al. "Beta Amyloid is Neurotoxic in Hippocampal Slice Cultures," The Neurobiology of				
	CZ	Aging, 16(5): 779-789, (1995)				
	DA	Hart et al., "Overproduction of perlecan core protein in cultured cells and transgenic mice", J.				
		Pathol., 194(2):262-269 (2001)				
DB		Hashimoto et al., "Tannins and Related Compounds. XC. 8-C-Ascorbyl (-)-Epigallocatechin 3-O-				
		Gallate and Novel Dimeric Flavan-3-ols, Oolonghomobisflavans A and B, from Oolong Tea," Chem. Pharm. Bull. 37(12):3255-3263 (1989)				
		Hashimoto et al., "Human recombinant NACP/α-synuclein is aggregated and fibrillated in vitro:				
	DC	Relevance for Lewy body disease," Brain Res. 799:301-306, (1998)				
		Hemingway et al, "Linkage Isomerism in Trimeric and Polymeric 2,3-cis-Procyanidins," J. Chem.				
	DD	Soc. Perkins Trans. 1:1209-1216 (1982)				

Date Considered				
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EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.				

Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Atorney Docket No. 17170-004001(25835-4003)	Application No. 10/684,178
List of Patents and Publications for Applicant's Information Disclosure Statement		Applicant Gerardo M. Castillo et al.	
		Filing Date October 10, 2003	Group Art Unit 1615

(37 CFR §1.98	3(b))			
		ocuments (include Author, Title, Date, and Place of Publication)		
Examiner Initial	Desig. ID	Document		
	DE	Hertel et al., "Inhibition of the electrostatic interaction between J-amyloid peptide and membranes prevents J-amyloid-induced toxicity," Proc. Natl. Acad. Sci. USA 94: 9412-9416 (1997)		
	DF	Hsiao et al., "Correlative Memory Deficits, Aβ Elevation, and Amyloid Plaques in Transgenic Mice," Science 274:99-102 (1996)		
	DG	Ishii et al., "Studies on the Chemical Constituents of Rutaceous Plants. XLIX. Development of a Versatile Method for the Synthesis of Antitumor-Active Benzo[c]phenanthridine Alkaloids. (1) Preparation of Various 2,4-Bisaryl-4-oxo-butyronitriles and 2,4-Bisaryl-4-oxo-butyramides," Chem. Pharm. Bull. 31(9):3024-3038 (1983)		
	DH	Ishimaru et al, :Flavan-2-ol and Procyanidin Glycosides from Quercus Miyagii," Phytochemistry 26:1167-1170, (1987)		
	DI	Janson et al., "Human Islet Amyloid Polypeptide (hIAPP) Cytotoxicity is caused by Membrane Damage," Diabetes 47:A250 (1998)		
	DJ	Johnson et al. "Islet Amyloid Polypeptide: Mechanisms of Amyloidogenesis in the Pancreatic Islet and Potential Roles in Diabetes Mellitus," Laboratory Investigation, 66(5): 522-534, (1992)		
	DK	Johnson et al. "Islet Amyloid, Islet-Amyloid Polypeptide, and Diabetes Mellitus," The New England Journal of Medicine, 321(8): 513-518, (1989)		
	DL	Jones et al, "The Condensed Tannins of Pasture Legume Species," Photochemistry, 15:1407-1409 (1976)		
	DM	Jucker et al., "Age-related deposition of glia-associated fibrillar material in brains of C57BL/6 mice", Neuroscience, 60(4):875-889 (1994)		
	DN	Kahn et al., "Evidence of Cosecretion of Islet Amyloid Polypeptide and Insulin by β-Cells," Diabetes 39:634-638 (1990)		
	DO	Kamei et al. "Amyloidosis Associated with Juvenile Rheumatoid Arthritis," Acta Pathol. Jpn., 32(1):123-133 (1982)		
100/100	DP	Kawamoto et al., "O-Benzylation of Phloroglucinol via Phloroglucinol Triacetate," Synthetic Communications 26(3):531-534 (1996)		
	DQ	Kitaguchi et al. "Novel Precursor of Alzheimer's Disease Amyloid Protein Shows Protease Inhibitory Activity," Nature, 331:530-532, (1988)		
	DR	Klunk et al., "Quantifying Amyloid β-Peptide (Aβ) Aggregation Using the Congo Red-Aβ (CR-Aβ) Spectrophotometric Assay," Analytical Biochemistry 266:66-76 (1999)		
	DS	Kosik et al. "MicrotubuleAssociated Protein Tau is a Major Antigenic Component of Pairedd Helicule Filaments in Alzheimer's Disease," Proc. Natl. Acad. Sci. USA, 83:4044-4048 (1986)		
-	DT	Krüger et al., "Ala30Pro mutation in the gene encoding I-synuclein in Parkinson's disease," Nature Genet. 18:106-108, (1998)		
	DU	Kubicova et al., "Synthesis of N,N'-Diarylalkanediamides and Their Antimycobacterial and Antialgal Activity," Molecules 5:714-726 (2000)		
	DV	Lee et al. "A68: A Major Subunit of Paired Helical Filaments and Derivatized Forms of Normal Tau," Science, 251: 675-678, (1991)		
	DW	Levine. "Thioflavine T interaction with synthetic alzheimer's disease B-amyloid peptides: Detection of amyloid aggregation in solution." Protein Science, 2:404-410, (1993)		
	DX	Levine. "Thioflavine T interacton with amyloid B-sheet structures. "Amyloid: Int. J. Exp. Clin. Invest. 2:1-6, (1995)		

Examiner Signature	Date Considered
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Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Atomey Docket No. 17170-004001(25835-4003)	Application No. 10/684,178
List of Patents and Publications for Applicant's Information Disclosure Statement		Applicant Gerardo M. Castillo et al	
		Filing Date October 10, 2003	Group Art Unit 1615
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(37 CFR §1.98	B(b))		
	Other D	ocuments (include Author, Title, Date, and Place of Publication)	
Examiner Initial	Desig. ID	Document	
	DY	Lewy et al., "Die angeborenen Defekte und Entwickelungs-storungen des Gehirns," in Handbuch der Neurologie, Berlin:Springer-Verlag pp.920-933 (1912) [in German]	
	DZ	Lorenzo et al, "Pancreatic islet cell toxicity of amylin associated with type-2 diabetes mellitus," Nature 368:756-760, (1994)	
	EA	Mandybur et al. "Cerebral Amyloid Angiopathy: The Vascular Pathology and Complications," Journal of Neuropathology and Experimental Neurology, 45(1): 79-90, (1986).	
	EB	Maresh et al., "Detection and quantitation of perlecan mRNA levels in Alzheimer's disease a normal aged hippocampus by competitive reverse transcription-polymerase chain reaction", J. Neurochem., 67(3):1132-1144 (1996)	
	EC	Masters et al. "Amyloid Plaque Core Protein in Alzheimers Disease and Down Syndrome," Proc. Natl. Acad. Sci. USA 82:4245-4249 (1983)	
	ED	Matsui et al., "Synthesis and Characterization of Fluorescent 4,6-Disubstituted-3-cyano-2-methylpyridines," J. Chem. Soc. Perkins. Trans. 2, pp201-206 (1992)	
	EE	Matthews et al, "Method for estimation of Proanthocyanidins based on their acid depolymerization in the presence of nucleophiles," J. Agric. Food Chem. 45:1195-1201, (1997)	
	EF	Mattice et al, "Molecular weight averages and 13C NMR intensities provide evidence for branching in proanthocyanidin polymers," Phytochem. 23(6):1309-1311, (1984)	
	EG	McAdam et al. "Association of Amyloidosis with Erythema Nodosum Leprosum Reactions and Recurrent Neutrophil Leucocytosis in Leprosy," The Lancet, pp. 572-576, Sep. 27, 1975.	
	EH	Metaxas et al. "Familial Mediterranean Fever and Amyloidosis," Kidney International, 20:676-685, (1981)	
	EI	Miller et al., "Localization of perlecan (or a perlecan-related macromolecule) to isolated microglia i vitro and to microglia/macrophages following infusion of beta-amyloid protein into rodent hippocampus", Gila, 21(2):228-243 (1997)	
	EJ	Morimoto et al, "Tannins and Related Compounds. LXI.1) Isolation and Structure of Novel Bi- and Triflavanoids from the leaves of Cassia fistula L.," Chem. Pharma. Bull. 36:39-47, (1988)	
	EK	Murray et al., "Synucleinopathies: a pathological and molecular review," Clinical Neuroscience Research 1:445-455 (2001)	
	EL	Murrell et al. "A mutation in the amyloid recursor protein associated with hereditary alzheimer's disease." Science, 254: 97-99 (1991)	
	EM	Nahri et al. "Both familial Parkinson's disease mutations accelerate I-Synuclein aggregation," J. Biol. Chem. 274:9843-9846 (1999)	
-	EN	Naiki et al. "Kinetic analysis of amyloid Fibril polymerization in vitro." Laboratory Investigation, 65(1):104-110, (1991)	
	EO	Naiki, H. and K. Nakakuki, "First-order kinetic model of Alzheimer's J-amyloid fibril extension in	

Examiner Signature	Date Considered
EXAMINER: Initial if citation considered, whether or not citation is in confirmance and act considered land depend on the confirmance and act conf	

Nay et al., "Gram-scale Production and Applications of Optically Pure 13C-Labelled (+)-Catechin

Nochlin et al., "Familial dementia with PrP-positive amyloid plaques: A variant of Gerstmann-

Niwano et al., "Inhibitory action of amyloid precursor protein against human Hageman factor (factor

vitro, "Laboratory investigation, 74(2):374-383 (1996)

Sträussler syndrome," Neurology 39:910-918 (1989)

XII)," J. Lab. Clin. Med. 125:251-6 (1995)

and (-)-Epicatechin," Eur. J. Org. Chem. pp. 2379-2384 (2001)

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(37 CFR &1 98/b))			

(37 CFR §1.98		
		ocuments (include Author, Title, Date, and Place of Publication)
Examiner Initial	Desig. ID	Document
	ES	Nonaka et al, "Tannins and Related Compound. XV.1) A New Class of Dimeric Flavan-3-ol Gallates, Theasinensins A and B, and Proanthocyanidin Gallates from Green Tea Leaf. (1)," Chem. Pharm. Bull. 31:3906-3914, (1983)
	ET	Pardridge et al. "Amyloid Angiopathy of Alzheimer's Disease: Amino Acid Composition and Partial Sequence of a 4,200-Dalton Peptid Isolated from Cortical Microvessels," Journal of Neurochemisty, 49(5): 1394-1401, (1987)
	EU	Pearl et al., "Reactions of Vanillin and Its Dervied Compounds. XXIX. 3,3',4,4'-Tetrahydroxy-benzil and Its Reduction," J. Org. Chem. 25:1449-1450 (1960)
	EV	Piao et al., "Co-localization of α-synuclein and phosphorylated tau in neuronal and glial cytoplasmic inclusions in a patient with multiple system atrophy of long duration," Acta Neuropathol. 101:285-293 (2001)
	EW	Pike et al. "In Vitro Aging of J-Amyloid Protein Cause Peptide Aggregation and Neurotoxity," Brain Research, 563:311-314, (1991)
	EX	Pike et al. "Structure-Activity Analyses of J-Amyloid Peptides: Contributions of the J25-35 Region to Aggregation and Neurotoxicity," Journal of Neurochemistry, 64(1): 253-265, (1995)
	EY	Pollanen et al., "Pathology and Biology of the Lewy Body," Journal of Neuropathology and Experimental Neurology 52(3):183-191 (1993)
	EZ	Polymeropoulos et al., "Mutation in the α-Synuclein Gene Identified in Families with Parkinson's Disease", Science, 276:2045-2047 (1997)
	FA	Ponte et al. "A New A4 Amyloid mRNA Contains a Domain Homologous to Serine Proteinase Inhibitors," Nature, 311:525-527, (1988)
	FB	Porter et al, "Isolation of three naturally occurring O-J-glucopyranodsides of procyanidin polymers," Phytochemistry 24:567-569, (1985)
	FC	Porter, L.J, "Flavans and proanthocyanidins," Chapter 2 in Flavans and proanthocyanidins Advances in Research since 1986, J B Harborne (Ed.) London: Chapman and Hall pp. 23-55, 1994
	FD	Porter, J.J., "Flavans and proanthocyanidins," Chapter 2 in The FlavanoidsAdvances in Research since 1980, JB Harborne (Ed.), London: Chapman and Hall, pp. 21-62, 1988
	FE	Prieur et al, "Oligomeric and polymeric procyanidins from grape seeds," Phyochem. 36:781-784, 1994
	FF	Puchtler et al., "On the Binding of Congo Red by Amyloid," J. Histochem. Cytochem. 10:355-364 (1962)
	FG	Santos-Buelga, C. and A. Scalbert, "Proanthocyanidins and tannin-like compounds – nature, occurrence, dietry intake and effects on nutrition and health," J. Sci Food Agri. 80: 1094-1117, (2000)
	FH	Saraiva et al. "Amyloid Fibral Protein in Familial Amyloidotic Polyneurotherapy, Portugese Type," J. Clin. Invest. 74:104-119 (1984)
. *14	FI	Saraiva et al. "Studies on Plasma Transthyretin (Prealbinum) in Familial Amyloidotic Polyneropathy, Portugese Type," J. Lab. Clin. Med. 102(4): 590-603, (1983)
	FJ	Sekiguchi et al., "Characterization of proteoglycans synthesized by murine embryonal carcinoma cells (P19) reveals increased expression of perlecan (heparan sulfate proteoglycan) during neuronal differentiation", J. Neurosci. Res., 38(6):670-686 (1994)

Examiner Signature	Date Considered
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EXAMINER: Initial if citation considered, whether or not citation is in co	onformance with MPEP 609: Draw line through citation if not in
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		ocuments (include Author, 1	Title, Date, and Place o	f Publication)
Examiner Initial	Desig. ID		Document	
	FK	Skinner et al. "The Prealbinum Nature (FAP)-Swedish Variety," Biochemica 1332, (1981)		
	FL	Snow et al, "Heparin modulates the co arterial smooth muscle cells, " Am J P	Pathol. 137(2): 313-30 (1990)	
	FM	Snow et al, "Time-related increase of carcinogenesis in the rat duodenal epi	thelium," Cell Biol Int Rep. 7(3)	:195 (1983)
	FN	Snow et al. "A close ultrastructural refibrils," Lab Invest. 57(6): 687-98 (19	987)	
	FO	Snow et al. "A temporal and ultrastructural relationship between heparan sulfate proteoglycans and AA amyloid in experimental amyloidosis," J. Histochem Cytochem. 39(10): 1321-30 (1991)		
	FP	Snow et al. "Cationic dyes reveal proteoglycans structurally integrated within the characteristic lesions of Alzheimer's disease," Acta Neuropathol 78(2): 113-23		
	FQ	Snow et al. "Characterization of tissue amyloidosis and acute inflammation. (75 (1987)		
	FR	Snow et al. "Congo red staining on 1 and Alzheimer 's disease and related disor	micron de-plasticized sections fo ders. " Prog Clin Biol Res. 317:3	or detection of lesions in 383-91 (1989)
	FS	Snow et al. "Early accumulation of he containing lesions of Alzheimer 's disc (1990)	paran sulfate in neurons and in t ease and Down 's syndrome. " A	he beta-amyloid protein- m J Pathol. 137(5): 1253-70
	FT	Snow et al. "Electrophoresis of glycos evidence for the presence of a heparin	-like molecule," Biomed Biochi	m Acta 46(7): 537-46 (1987)
	FU	Snow et al. "Immunolocalization of he plaques of Gerstmann-Straussler synd 63(5): 601-611 (1990)	rome, Creutzfeldt-Jakob disease	and scrapie," Lab Invest.
	FV	Snow et al. "Morphometric study of the rat duodenal epithelium during the initial six months of 1,2-imethylhydrazine carcinogenesis, Cancer Res. 43(10):4838-48 (1983)		
	FW	Snow et al. "Sulfated glycosaminogly (1987)	cans in Alzheimer 's disease, " H	(um Pathol. 18(5): 506-10
	FX	Snow et al. "Sulfated glycosaminogly Neuropathol.77(4): 337-42 (1989)		
	FY	Snow et al. "Sulfated glycosaminogly 56(1): 120-3 (1987)		•
	FZ	Snow et al. "Temporal relationship be deposition during experimental amylo		

Examiner Signature	Date Considered
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EXAMINER: Initial if citation considered, whether or not citation is in co	
conformance and not considered. Include copy of this form with next co	mmunication to applicant.

Snow et al. "The presence of heparan sulfate proteoglycans in the neuritic plaques and congophilic angiopathy in Alzheimer's disease. "Am J Pathol. 133(3): 456-63 (1988)

Snow et al., "An important role of heparan sulfate proteoglycan (Perlecan) in a model system for the deposition and persistence of fibrillar AJ-amyloid in rat brain", Neuron., 12(1):219-234 (1994)

(1985)

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Substitute Form PTO-1449 U.S. Department of Commerce (Modified)

List of Patents and Publications for Applicant's Information Disclosure Statement

U.S. Department of Commerce Patent and Trademark Office

Atorney Docket No. 17170-004001(25835-4003)

Applicant Gerardo M. Castillo et al.

Filing Date Group Art Unit October 10, 2003

Group Art Unit 1615

(37 CFR §1.98(b))

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miliai	ID	Document  Snow et al. "Differential hinding of vaccular cell derived protectives (confessor highway)
	GC	Snow et al., "Differential binding of vascular cell-derived proteoglycans (perlecan, biglycan, decorin, and versican) to the beta-amyloid protein of Alzheimer's disease", Arch. Biochem.
	GC	
		Biophys., 320(1):84-95 (1995)
	GD	Snow et al., "Heparan sulfate proteoglycan in diffuse plaques of hippocampus but not of cerebellum
		in Alzheimer's disease brain", Am. J. Pathol., 144(2):337-347 (1994)  Snow et al., "Identification in immunolocalization of a new class of proteoglycan (keratan sulfate) to
	GE	the neuritic plaques of Alzheimer's disease", Exp. Neurol., 138(2):305-317 (1996)
		Snow et al., "In vitro and in vivo models to unravel the potential roles of Flavans and J/A4 in the
	GF	pathogenesis of Alzheimer's disease", Hippocampus, 3(Special Issue):257-268 (1993)
		Snow et al., "Peripheral distribution of dermatan sulfate proteoglycans (decorin) in amyloid
	GG	containing plaques and their presence in neurofibrillary tangles of Alzheimer's disease", J.
	40	Histochem Cytochem., 40(1):105-113 (1992)
		Snow, A. D., "Midwest summit on health care reform," Kansas Medicine 94(10): pp.258 and 272
	GH	(1993)
		Snow. "Proteoplycans in the pathogenesis of alzheimer's disease and other amyloidoses."
	GI	Neurobiology of Aging, 10:481-497, (1989)
		Spillantini et al., "I-Synuclein in filamentous inclusions in Lewy bodies from Parkinson's disease
	GJ	and dementia with Lewy bodies," Proc. Natl. Acad. Sci. USA. 95:6469-6473 (1998)
	<del> </del>	Steynberg et al., "Oligomeric flavanoids. Part 27. Interflavanyl bond formation in procyanidins
	GK	under neutral conditions," Tetrahedron 54:8153-8158 (1998)
		Tamura et al., "Studies on the inhibition of the Autoxidation of Oils and Fats. Part 6. The Syntheses
	GL	of some w, w'-bis(3,4-dihydroxyphenyl)alkanes (I)," Journal of the Agricultural Chemical Society
		of Japan (Nippon Nogei Kagakukaishi), 27: 491-498 (1953)
		Tamura et al., "Studies on the inhibition of the Autoxidation of Oils and Fats. Part 7. The Syntheses
	GM	of some w, w'-bis(3,4-dihydroxyphenyl)alkanes (2)," Journal of the Agricultural Chemical Society
		of Japan (Nippon Nogei Kagakukaishi), 27: 877-881 (1953)
•	CNI	Tanzi et al. "Protein Inhibitor Domain Encoded by an Amyloid Protein Precursor mRNA Associated
	GN	with Alzheimer's Disease," Nature, 331:528-532, (1988)
	GO	Tawara et al. "Amyloid Fibril Protein in Type 1 Familial Amyloidotic Polyneurotherapy in
	40	Japanese," J. Lab. Clin. Med., 98(6): 811-822, (1981)
	GP	Thompson et al, "Plant Proanthocyanidins. Part 1. Introduction; the Isolation, Structure, and
	Ur Ur	Distribution in Nature of Plant Procyanidins," J. Chem. Soc. Perkins Trans. 1: 1387-1399 (1972)
	GQ	Trojanowski et al., "Parkinson's Disease and Related Synucleinopathies are a New Class of Nervous
	uQ	System Amyloidoses," Neurotoxicology 23:457-460 (2002)
		Tückmantel, "Studies in Polyphenol Chemistry and Bioactivity. 1. Preparation of Building Blocks
	GR	from (+)-Catechin. Procyanidin Formation. Synthesis of the Cancer Cell Growth Inhibitor, 3-O-
		Galloyl-(2R,3R)-epicatechin-4J,8-[3-O-Galloyl-(2R,3R)-epicatechin]," J. Am. Chem. Soc.
		121:12073-12081 (1999)
	GS	Ueda et al., "Molecular cloning of cDNA encoding an unrecognized component of amyloid in
		Alzheimer 's disease, " Proc. Natl. Acad. Sci. USA 90:11282-11286 (1993)
	GT	Upton et al, "Novel 5,8-Diazabenzo[c]phenanthrenes: Synthesisand Mutagenicity," Journal of
		Pharmacy and Pharmacology 50(5): 475-482 (1998)

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Initial	ID	. Document
	GU	Van Broeckhoven et al. "Amyloid J Protein precursor gene and Hereditary cerebral hemorrage with amyloidosis (Dutch)." Science, 248:1120-1122 (1990)
	GV	Van der Eycken et al., "The Synthesis of 4-Desoxy-2-Azapodophyllotoxins," Tetrahedron Letters 30(29): 3873-3876 (1989
	GW	Verchere et al, "Islet amyloid formation associated with hyperglycemia in transgemic mice with pancreatic beta cell expression of human islet amyloid polypeptide," Proc. Natl. Acad. Sci. U.S.A. 93: 3492-3496, (1996)
_	GX	Vogel's Textbook of Practical Organic Chemistry, 5th ed. Furniss, B. S. et al. (Eds.), London: Longman Scientific & Technical; New York: John Wiley & Sons, 6.142:1044-1045 (1989)
	GY	Vogel's Textbook of Practical Organic Chemistry, 5th ed. Furniss, B. S. et al. (Eds.), London: Longman Scientific & Technical; New York: John Wiley & Sons, 6.143:1045-1046 (1989)
	GZ	Vogel's Textbook of Practical Organic Chemistry, 5th ed. Furniss, B. S. et al. (Eds.), London: Longman Scientific & Technical; New York: John Wiley & Sons, 6.139:1040-1041 (1989)
Wakabayashi et al., "Accumulation of α-Synu		Wakabayashi et al., "Accumulation of α-Synuclein/NACP is a cytopathological feature common to Lewy body disease and multiple system atrophy," Acta Neuropath 96: 445-452 (1998)
	НВ	Wattanasin et al, "An Improved Procedure for the Preparation of Chalcones and Related Enones," Synthesis 1980(8): 647-650 (1980)
	НС	Westermark et al., "Amyloid and polypeptide hormones: what is their interrelationship?," Amyloid: Int. J. Exp. Clin. Invest. 1:47-60 (1994)
-	HD	Westermark et al., "Quantitative Studies of Amyloid in the Islets of Langerhans," Upsala J. Med. Sci. 77:91-94 (1972)
	HE	Westermark et al., "The Influence of Amyloid Deposits on the Islet Volume in Maturity Onset Diabetes Mellitus," Diabetologica 15:417-421 (1978)
	HF	WHO-IUIS Nomenclature Sub-Committee, "Nomenclature of amyloid and amyloidosis," Bulletin of the World Health Organization, 71(1): 105-108 (1993).
	HG	Williard et al., "Boron Trihalide-Methyl Sulfide Complexes as Convenient Reagents for Dealkylation of Aryl Ethers," Tetrahedron Letters 21:3731 -3734 (1980)
	нн	Wood et al., "I-synuclein fibrillogenesis is nucleation-dependent," J. Biol. Chem. 274:19509-19512, (1999)
	HI	Zhang et al, "Potentillanin, A Biflavanoid and a procyanidin glycoside from potentilla viscosa," Phytochemistry 27:3277-3280, (1988)

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